Concomitant Beta Thalassemia Trait and Iron Deficiency Anemia in Pregnancy.

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Abstract: Thalassemia syndromes and iron deficiency anemia (IDA) are the two most common etiologies of microcytic hypochromic anemia in children and adults. It has long been considered that iron deficiency does not exist in thalassemia syndromes, including thalassemia major as well as trait. However, studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait (BTT). Earlier authors have demonstrated lower initial hemoglobin levels in patients with coexisting IDA and BTT. This has been explained by the lack of hemopoietic nutrients due to iron deficiency superimposing on the imbalance in globin chain synthesis. This case report showed that the concomitant existence of beta thalassemia minor and iron deficiency anemia in pregnancy. The evaluation of anemia in pregnancy is a tricky subject and is essential to treat. This case showed a normal HbA2 (<3.5%) finding in a patient with beta thalassemia minor with concomitant iron deficiency anemia leading to difficulty in diagnosing beta thalassemia in patients. The combination of these two anemias along with anemia of pregnancy can justify the severe anemia seen in this patient.

Keywords: Microcytic Hypochromic Anemia, Beta Thalassemia Trait (BTT), Hemopoietic.
The hemoglobinopathies should be evaluated further with hemoglobin electrophoresis. High Performance Liquid Chromatography which is also known as High Pressure Liquid Chromatography. It is a popular analytical technique used for the separation, identification and quantification of each constituent of mixture. HPLC is an advanced technique of column liquid chromatography. The solvent usually flows through column with the help of gravity but in HPLC technique the solvent will be forced under high pressures upto 400 atmospheres so that sample can be separated into different constituents with the help of difference in relative affinities[5-11].
In a study conducted by Rachna Khera et al., used High-performance liquid chromatography (HPLC) is a technique introduced for the accurate diagnosis of hemoglobinopathies and thalassemias. The advantage of the HPLC system is the excellent resolution, reproducibility, & quantification of several normal & abnormal hemoglobin resulting in accurate diagnosis of thalassemia syndromes. The study evaluated the use of HPLC technique in diagnosis of thalassemia syndromes and also correlate it with clinicohematological profile in these cases. The results of the study are shown in the table [12].

### Hemoglobin profile in each case obtained on HPLC (mean ± SD, range)

<table>
<thead>
<tr>
<th>Presumptive HPLC diagnosis (no. of cases)</th>
<th>Hb A (%) (range)</th>
<th>Hb F (%)</th>
<th>HbA2 (%)</th>
<th>Variant Hb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-thal trait (62)</strong></td>
<td>83.6 ± 2.7 (71.7–89.1)</td>
<td>1.5 ± 1.2 (0.2–4.9)</td>
<td>5.7 ± 0.9 (4.0–8.2)</td>
<td></td>
</tr>
<tr>
<td><strong>β-thal major (6)</strong></td>
<td>25.0 ± 22.7 (4.6–60.5)</td>
<td>65.8 ± 29.8 (30.6–91.1)</td>
<td>2.8 ± 1.5 (0.4–5.5)</td>
<td></td>
</tr>
<tr>
<td><strong>β-thal intermedia (5)</strong></td>
<td>30.4 ± 31.6 (0.5–65.9)</td>
<td>62.6 ± 37 (22–98)</td>
<td>5.5 ± 2.6 (2.1–8.2)</td>
<td></td>
</tr>
<tr>
<td>HbS/β-thal (2)</td>
<td>1.6 ± 2.8 (1.4–1.8)</td>
<td>19.3 ± 9.4 (14.2–24.3)</td>
<td>5.0 ± 0.6 (4.9–5.1)</td>
<td>74.1 ± 7.8 (69.2–79.5)</td>
</tr>
<tr>
<td>HbE/β-thal (8)</td>
<td>24.1 ± 18.1 (65.5–47.2)</td>
<td>18.7 ± 22.2 (1.4–33.2)</td>
<td>–</td>
<td>52.8 ± 17.9 (34.2–60.9)</td>
</tr>
<tr>
<td>HbB disease (4)</td>
<td>88.1 ± 6.9 (81.5–93.3)</td>
<td>0.8 ± 0.6 (0.2–1.8)</td>
<td>2.6 ± 0.6 (2–3.4)</td>
<td></td>
</tr>
<tr>
<td>Sickle cell trait (1)</td>
<td>46.3</td>
<td>12</td>
<td>6.9</td>
<td>33.8</td>
</tr>
<tr>
<td>Hemoglobin Sickle cell ds (1)</td>
<td>0</td>
<td>98</td>
<td>3.1</td>
<td>85.7</td>
</tr>
<tr>
<td>HbE-trait (7)</td>
<td>62.3 ± 2.7 (59.8–67.7)</td>
<td>0.96 ± 0.7 (0.4–2.3)</td>
<td>0</td>
<td>28.2 ± 5.0 (17–31.2)</td>
</tr>
<tr>
<td>Hemoglobin HbE &amp; ds (1)</td>
<td>4.0</td>
<td>0.7</td>
<td>0</td>
<td>93.7</td>
</tr>
<tr>
<td>HbD-Punjab trait (8)</td>
<td>54.5 ± 6.3 (50.7–77)</td>
<td>0.6 ± 0.4 (0.2–1.2)</td>
<td>1.4 ± 0.4 (0.7–1.8)</td>
<td>34.8 ± 8.0 (18.3–38.5)</td>
</tr>
<tr>
<td>Hemozoon HbD &amp; ds (1)</td>
<td>5.0</td>
<td>12</td>
<td>2.1</td>
<td>86.5</td>
</tr>
<tr>
<td>Double hetero HbE &amp; ds (1)</td>
<td>1.4</td>
<td>0.4</td>
<td>6(ES)</td>
<td>30.7</td>
</tr>
<tr>
<td>HbD-thal trait (1)</td>
<td>45.1</td>
<td>0.8</td>
<td>0</td>
<td>43.3</td>
</tr>
<tr>
<td>Hb J Oxford (2)</td>
<td>72.5 ± 8.3 (66.4–78.6)</td>
<td>2.3 ± 2 (0.8–3.7)</td>
<td>1.9 ± 0.1 (0.9)</td>
<td>18.2 ± 4 (15.3–21)</td>
</tr>
</tbody>
</table>

β-thalassemia minor represents the heterozygous state. In general, a heterozygote for thalassemia is diagnosed with a mild anemia (hemoglobin A level 1 or 2 g below normal range), low mean cell volume, low mean corpuscular hemoglobin, elevated hemoglobin A2, and normal or elevated hemoglobin F.

During pregnancy, women with thalassemia minor will often show more significant anemia, which is often most prominent during the latter half of the second trimester and early third trimester [13-16]. In a study
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Conducted by Amoee S et.al showed that β-thalassemia minor does not significantly influence the pregnancy outcome in the negative way in terms of Cesarean delivery, hypertensive disorders, gestational diabetes mellitus, premature rupture of membranes and preterm labor.

Globally, the commonest cause for anemia in pregnancy is IDA. The Nutrition Impact Model Study, a systematic analysis of 257 population-representative data sources from 107 countries, estimated the global prevalence of anemia in pregnancy as 43% in 1995 and 38% in 2011 with the range varying from 17% in developed and 56.4% in developing countries.

During pregnancy, the total blood volume increases by about 1.5 liters, mainly to supply the demands of the new vascular bed and to compensate for blood loss occurring at delivery [17].

Red cell mass (driven by an increase in maternal erythropoietin production) also increases, but relatively less, compared with the increase in plasma volume, the net result being a dip in hemoglobin concentration. The drop in hemoglobin is typically by 1–2 g/dL by the late second trimester and stabilizes thereafter in the third trimester.

White blood cell count is increased in pregnancy with the lower limit of the reference range being typically 6,000/cumm. Leucocytosis, occurring during pregnancy is due to the physiologic stress induced by the pregnant state [18].

Large cross-sectional studies done in pregnancy of healthy women (specifically excluding any with hypertension) have shown that the platelet count does decrease during pregnancy, particularly in the third trimester. This is termed as “gestational thrombocytopenia.” It is partly due to hemodilution and partly due to increased platelet activation and accelerated clearance [19].

CASE PRESENTATION

A 26 year old female with 32 weeks pregnancy presented to outpatient department with complaints of shortness of breath and fatigue for past two weeks. The shortness of breath was gradual in onset, present at rest, increased on exertion. It was not associated with chest pain, cough, orthopnea, paroxysmal nocturnal dyspnea, fever. She developed fatigue gradually. No decrease in appetite, no weight loss, no bleeding episodes.

Past history- No significant past history.

Personal history- Normal bladder and bowel.
Non- vegetarian diet.
No smoking, alcohol or illicit drug use.

Menstrual history- Amenorrhea for past 8 months, menarche at 14 years age, regular, soaks 2-3 pads per day, last for 3-5 days.

Family history- Thalassemia minor in father.

EXAMINATION- Patient lying comfortably in bed.
Patient conscious, Oriented to time/place and person.
Pallor present/ no icterus/ no cyanosis/no clubbing/no lymphadenopathy.
Concomitant Beta Thalassmia Trait and Iron Deficiency Anemia in Pregnancy.

**Vitals:** BP- 110/70 mmhg  
PR- 98/min  
RR-22/min  
SpO2-98%

**Systemic:** CVS- S1/S2 normal, no additional heart sound.  
RESPIRATORY- Bilateral air entry clear, no additional sound.  
CNS- Within normal limit.  
Abdominal- Soft, 32 weeks gestation, FHS 140/min.

**INVESTIGATION:**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-pregnancy</th>
<th>pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>11.6</td>
<td>4.6</td>
</tr>
<tr>
<td>MCV</td>
<td>80</td>
<td>76</td>
</tr>
<tr>
<td>RDW</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Mentzer Index</td>
<td>19</td>
<td>34</td>
</tr>
<tr>
<td>TLC</td>
<td>4400</td>
<td>4000</td>
</tr>
<tr>
<td>RBC</td>
<td>4.1</td>
<td>2.2</td>
</tr>
<tr>
<td>S. Ferritin</td>
<td>113</td>
<td>35</td>
</tr>
<tr>
<td>S. Iron</td>
<td>160</td>
<td>56</td>
</tr>
<tr>
<td>TIBC</td>
<td>323</td>
<td>486</td>
</tr>
<tr>
<td>Platelet</td>
<td>2.8</td>
<td>1.98</td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**HPLC FINDINGS**

<table>
<thead>
<tr>
<th>Hb F</th>
<th>2.8%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb A</td>
<td>92%</td>
</tr>
<tr>
<td>Hb A2</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

Bone marrow biopsy- Normal  
Peripheral smear- Hypochromic microcytic anemia

**II. Conclusion**

Thalassemia syndromes and iron deficiency anemia (IDA) are the two most common etiologies of microcytic hypochromic anemia in children and adults. It has long been considered that iron deficiency does not exist in thalassemia syndromes, including thalassemia major as well as trait. However, studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait (BTT). Earlier authors have demonstrated lower initial hemoglobin levels in patients with coexisting IDA and BTT \[20-22\]. This has been explained by the lack of hemopoietic nutrients due to iron deficiency superimposing on the imbalance in globin chain synthesis \[23\]. Similar changes have also been shown in other red cell parameters, serum iron, ferritin, and total iron binding capacity. These changes have also been demonstrated to improve after adequate iron replacement therapy \[21, 22, 24\].

HbA2 levels have been reported to be lower in patients with coexisting IDA and BTT, with improvement in levels after iron therapy \[20, 25\]. However, other studies have shown no significant difference in HbA2 levels in such patients \[26, 27\]. The reduction in HbA2 levels in patients with concomitant BTT and IDA has been suggested to interfere in the diagnosis of the former. A recent study has hypothesized that such an occurrence can lead to these patients with BTT marrying another person with BTT with attendant risk of birth of thalassemia major child \[28\].
An extensive search of the available indexed English literature yielded only few Indian reports of concomitant BTT and iron deficiency [23, 29-31].

This case report showed that the concomitant existence of beta thalassemia minor and iron deficiency anemia in pregnancy. The evaluation of anemia in pregnancy is a tricky subject and is essential to treat. This case showed a normal HbA₂(<3.5%) finding in a patient with beta thalassemia minor with concomitant iron deficiency anemia leading to difficulty in diagnosing beta thalassemia in patients. The combination of these two anemias along with anemia of pregnancy can justify the severe anemia seen in this patient.

In a study conducted by Sarika Verma et.al showed the changes in blood parameters in patients with concomitant beta thalassemia minor and iron deficiency anemia. In the study the mean hemoglobin level rose to g/dL and this difference was statistically significant (P<0.001). Similarly, serum iron levels rose to a mean of μg/dL with statistically significant difference (P<0.001). Serum ferritin also showed a significant increase after therapy, while TIBC reduced.

HbF levels remained largely unchanged after iron therapy while HbA₂ values showed significant rise after therapy (P<0.04).

References


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